CERTIFICATE OF MAILING
37 C.F.R. § 1.8

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April 19, 2004
Date

Shelley P.M. Fussey

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Hills, Woodcock & Staniforth

Serial No.: 09/856,400

Filed: May 22, 2001

For: Anti-Asthmatic Combinations Comprising Surface Active Phospholipids

Group Art Unit: 1616

Examiner: M. Haghighatian

Atty. Dkt. No.: 4040.000300

DECLARATION OF
ROBERT PRICE UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, ROBERT PRICE, HEREBY DECLARE AS FOLLOWS:

1. I hold the position of Lecturer in Pharmaceutical Sciences at The University of Bath, of Bath, U.K. I have held this position for about two and a half years. Prior to my present employment, I held the position of Post-Doctoral Research Assistant, also at The University of Bath, U.K. My research expertise is primarily in the fields of pharmaceutical surface science and

particle engineering in pulmonary drug delivery. A copy of my *curriculum vitae* is attached hereto as Exhibit A.

2. I reside in England and am a British subject. I act as a paid consultant for the assignee of the captioned patent application in my area of expertise.

3. I worked with one of the inventors, John Staniforth, when I was employed as Post-Doctoral Research Assistant in 1999 and 2000.

4. I have studied the specification and claims of the captioned patent application. I have been advised that the relevant dates of the captioned patent application are the international filing date of November 26, 1999 and the priority dates of May, 1999 and November 26, 1998.

5. I understand the present invention, as disclosed and claimed in the captioned patent application, to concern products and methods for preventing or treating asthma. In particular, I understand the present invention to concern the use, in combination, of a surface active phospholipid composition and an antiasthma drug. In addition, the invention involves the use of large doses of the phospholipid composition. The use of the large, individually inhalable doses introduced into the lung at one time leads to the formation of a barrier layer of the phospholipids over the surfaces of the airways. The phospholipid spreads across the airway surfaces and forms, in the quantity administered, a relatively thick barrier coating or wall over the airway surfaces. Some binding to the epithelium also occurs. The phospholipids composition used in accordance with the invention may involve two possible mechanisms for improvement of the effectiveness of antiasthma therapy. Firstly, the therapeutic benefit of the phospholipids composition itself

will allow the dosage of a given antiasthma drug to be reduced, with commensurate reduction in the extent and/or severity of the side effects of the antiasthma drug. Secondly, the phospholipids can alleviate the drug side effects per se. Irrespective of the precise mode of action of the integers of the product, however, the invention allows for the desired clinical effect to be obtained using a reduced amount of antiasthma drug – that is, the effect of the antiasthma drug is enhanced. Therefore, the invention provides important new therapeutic compositions and their use, with advantages such as comfort and ease of use for the user and reduced side effects of the antiasthma drug (through available reductions in the required doses thereof.)

6. I have studied the second Official Action dated 16th June, 2003 issued by the U.S. Patent and Trademark Office (P.T.O.) in regard to the captioned patent application. I have also studied the first Official Action dated 2nd October, 2002, earlier issued by the P.T.O. for this application.

7. I have also studied the documents cited in the Official Actions, U.S. Patent No. 4,895,719 by Radhakrishnan *et al.*, U.S. Patent No. 5,306,483 by Mautone, U.S. Patent No. 5,925,334 by Rubin & Newhouse and PCT application No. WO 96/19199 by Bystrom. I refer to these documents below as "Radhakrishnan", "Mautone", "Rubin" and "Bystrom", and I have focused my study on Radhakrishnan, Mautone and Rubin.

8. I understand that the P.T.O. has taken the position that the invention as defined by the claims of the captioned patent application would have been obvious to someone working in this field of study at the relevant dates in the light of Radhakrishnan, Mautone and Rubin, when viewed in combination.

9. Firstly, I would like to point out that it would not have been an obvious step to one skilled in the art to have combined the disclosure of Radhakrishnan with Mautone or with Rubin. Radhakrishnan is concerned with making liposomal compositions for delivering therapeutic substances, and more specifically with modifying the composition of the lipid shell of the liposome to control the release of the encapsulated therapeutic substance. Radhakrishnan thus relates to encapsulation of the therapeutic substance in a liposome which is moreover to have precisely controlled characteristics. Mautone on the other hand is concerned with obtaining very rapid spreading of a phospholipid composition, and it would have been thought counter-productive to combine the teaching of Mautone (rapid but essentially uncontrolled spreading) with Radhakrishnan (controlled composition of liposome to achieve release of active material in a controlled manner).

10. Also, the combination of Radhakrishnan with Rubin would not have been reasonably considered by one skilled in the art. The ratio of therapeutic agent to lipids is important in Radhakrishnan because it is key to the objective of controlling release from the liposomes. Significantly increasing the amount of lipid material would clearly result in significantly lowering the amount of encapsulated drug, leading to poor dose reproducibility. That would have been immediately apparent, and combination of Radhakrishnan with Rubin would not have been contemplated.

11. I disagree with the assessment that Radhakrishnan, Mautone and Rubin, even if viewed in combination, would have rendered the claims in the captioned patent application obvious to someone working in this field of research at the relevant dates.

12. I am providing this declaration to explain the reasons, based upon the evidence discussed below, why Radhakrishnan, Mautone and Rubin, either separately or in combination, would not have taught or suggested the invention disclosed and claimed in the captioned patent application to a person with an ordinary level of skill who was working in this field of study at the relevant dates. For example, I explain why such a person would not reasonably expect, by following the methods described in the cited references or routine variations of such methods, to obtain a simple and effective antiasthma treatment permitting enhanced compliance and patient comfort, to enable reduced dosages of antiasthma drug to be used, thereby reducing problematic side effects in patients.

13. Below, I explain that Radhakrishnan, Mautone and Rubin, either separately or in combination, do not teach or suggest important features of the present invention, such as the high dosages of phospholipid and the formation of a relatively thick barrier coating. I also explain that the use of a combination of high phospholipid doses and an antiasthma drug is not taught or suggested in the three documents and that a person with an ordinary level of skill working in this field at the relevant dates would not have reasonably expected to achieve "enhanced" effect of the antiasthma drug (as described in paragraph 5) due, in part, to the belief at the time that phospholipids in phospholipid/drug combinations were essentially to be regarded as mere vehicles for delivery of a drug component and/or as mere surfactants. Thus, the advance of recognising that a phospholipid composition according to the invention might itself contribute in the alleviation of asthma (over and above effects based on merely reducing surface tension), and provide a means of enhancing the activity of an antiasthma drug was made only by the inventors and is a surprising advance in this field.

14. Before I discuss Radhakrishnan, Mautone and Rubin, I will briefly review what was known about lung surfactants at the relevant dates. I consider that this information would be part of the knowledge which was generally known and accepted in the field from about 26 November 1998 to about 26 November 1999.

15. As recited on page 1 of the Application, surface active phospholipid compositions are used widely to treat respiratory distress syndrome in neonates. In that context, the need is to counteract the forces (primarily surface tension) which tend to close the finer airways and voids in the neonatal lung. The surfactant properties of, for example, dipalmitoylphosphatidylcholine (DPPC) which is often an ingredient of the compositions results in reduction of the surface tension and thus facilitates opening of the alveoli. The commercial product ALEC mentioned in the present application comprises DPPC and a phosphatidylglycerol (PG).

16. Certain surfactant compositions have been proposed for other clinical applications. In general, however, the surfactants have been administered in suspensions or dispersions, for example, using nebulisers or pressurised metered dose inhalers (PMDIs). The administration of surfactants or of other therapeutic agents from nebulisers can represent a significant problem because, for example, it may involve significant inconvenience and discomfort for the patient. The inconvenience and discomfort are related to the large dosing times which are involved for the large bolus deliveries for which nebulisers are typically used, with nebulisers being non-portable devices which will restrict the patient to home or hospital during the administration. Other problems are associated with the use of PMDIs. In particular, their use is constrained by the construction of the devices and the necessity for propellants. The metering valve of PMDIs limit the volume of suspension or solution that can be delivered, and thus restrict the amount of

active component. Commercially available meters can deliver about 100μl of liquid, and since the drug is in suspension or solution, it follows that the drug will represent only a minor proportion of the material that is actually metered. It follows that that represents a severe limitation on the amount of drug that can be delivered. In practice, those skilled in the art would consider the maximum amount of drug that can be delivered in a PMDI to be about 5mg. PMDIs also involve the problem of coordination of the actuation of the device with inhalation of the delivered aerosol. Many patients are unsuccessful at achieving such coordination with the consequence that reproducibility of the inhaled dose can be low.

17. In the light of this background, I have considered Radhakrishnan. Radhakrishnan is concerned with a system and method for administering a drug, at a selected dose, via the respiratory tract. According to Radhakrishnan, liposomes whose phospholipid components contain longer and/or more saturated acyl chain moieties have longer drug-release half-lives (col. 5, lines 10 to 12). He also states that "The most significant increases in drug release rates were observed when the liposomes contained a significant proportion of lipids whose transition temperatures are above the temperature at which the efflux half-lives are measured, e.g., 37+C." (col. 5, lines 16 to 20).

18. In summary, therefore, Radhakrishnan sets out (a) to provide a liposomal vehicle for delivery of a drug and (b) to modify the properties of the liposomes so as to control in a desired manner the release of the drug from the liposomes. It is in particular (b) upon which Radhakrishnan focuses.

19. The liposomal nature of the product of Radhakrishnan sets clear constraints upon the freedom of the skilled man to vary the various components of the product. Firstly, liposomes will only form under a very limited range of conditions relating to the lipid concentration in the aqueous medium in which they are formed. Secondly, the liposomes are, as already mentioned, conceived as a mere vehicle for the delivery of a drug. The amount of lipid present will therefore be regarded as variable only within the confines of what would not prejudice the effective and reproducible administration of the drug. That is, it is the dosage of the drug that is of overriding importance, and it cannot have been obvious to change the vehicle in a way which would be detrimental to the effective and reproducible administration of the drug. Indeed, such changes would have been contra-indicated to the typical person working in the field at the time.

20. Mautone concerns a process for preparing lipid crystals in combination with a therapeutically active agent. As noted in the Office Action of 16 June 2003 (see page 4), Mautone asserts that his lipid crystal vehicle system can deliver for example 5mg each DPPC:CP, DPPC:PG or DPPC:CP:PG (200:1, 7:1 or 7:0.35:1, w/w, respectively), which when delivered quantitatively covers 100% of the airspace surface in the lungs of normal adults. The lipid crystals of Mautone are clearly non-liposomal in nature.

21. It is abundantly clear from Mautone (see for example col. 3, lines 52 to 61) that Mautone is essentially seeking to use the surface active lipid merely to spread an accompanying active drug quickly over the lung surfaces. Mautone recognises the benefits of *inter alia* rapidly spreading, reduction of surface tension (see col. 4, lines 26 to 33) which were of course known per se before Mautone's invention and are not as I understand it part of Mautone's invention. Importantly, however, the objectives and advantages described in Mautone would be achievable

with a merely monomolecular film over the lung surfaces. Given that Mautone already asserts 100% coverage (col. 4, line 9 – see above), there is no motivation in Mautone to use large doses of phospholipid, for example 25mg or more. Mautone's lung formulations are delivered from PMDIs, and the dosages indicated in the Examples are fully consistent with the maximum dosages that are in practice achievable from such systems – see paragraph 16 above.

22. The lipid crystals of Mautone are not liposomes. That is clear *inter alia* from the fact that Mautone describes the material as being soluble in the propellant, the reference to solubility inherently excluding the possibility that liposomes are formed, which would be understood by one skilled in the art.

23. Rubin relates to results arising from a patient study in patients with chronic bronchitis, in which a synthetic surfactant, in suspension form, was administered to patients using a jet nebuliser used for 15 minutes, 3 times a day for 14 days. It is stated that patients were randomised to receive one of three different doses of surfactant, either 202.5mg DPPC/day, 607.5mg DDPC/day or 1215mg DPPC per day.

24. I am familiar with nebuliser apparatus of the kind used by Rubin. I am aware, and it is known in the field, that the dose actually inhaled by the patient is typically much lower than the dose nominally delivered by such devices. Thus, about 25% of the measured dose is typically lost in the nebuliser as a result of incomplete delivery, deposit on internal surfaces or leakage. Further, such devices deliver the material continuously so that, assuming inhalation takes up only 50% or less of the specified time, at least 50% of the delivered amount will be lost during exhalation. Whilst Rubin does not address those issues, one of skill would expect that the actual

daily doses delivered to the patient in Rubin were for those reasons much less than those indicated.

25. Nebuliser apparatus of the kind described by Rubin is, furthermore, highly unsatisfactory in terms of patient comfort, convenience and compliance, in view of the need for the patient to be connected for long periods of time to a machine that is not portable.

26. It would not have been obvious to a person of ordinary skill in the art to have modified the preparations of Radhakrishnan by adding the component ratios as taught by Mautone. As I have already mentioned, Radhakrishnan sets out to control the release of drug from liposomes. The approach of Mautone is completely different, seeking to have a rapidly spreading film of lipid to spread drug over the lung surfaces. There would have been no motivation to one skilled in the art reading Mautone to change the composition disclosed in Radhakrishnan, especially given the constraints imposed by the liposomal nature of Radhakrishnan's product and his objective of controlling release. Why should one skilled in the art seeking improved control of drug release according to Radhakrishnan, that is by means of controlling release of the drug from liposomes, seek to modify the disclosure in view of Mautone, which would apparently result in a product in which that control was lost?

27. Even if one skilled in the art had considered modifying Radhakrishnan in view of Mautone, he would not have arrived at the invention disclosed and claimed in the captioned patent application because Mautone fails to disclose the use of large doses of lipid.

28. In contrast to the suggestion on page 6 of the Office Action of 16 June 2003, it would not have been "obvious to one of ordinary skill in the art, given the teachings of the combined references on lower dosages of the phospholipids, to have looked in the art for higher doses, as taught by Rubin, in order to obtain more effective results, especially since Radhakrishnan teaches that effects of liposomes are dose-related."

29. Firstly, it seems inappropriate to refer to Radhakrishnan providing any teaching on dosages of the phospholipids components of the liposomes. Radhakrishnan is concerned with dosages of an incorporated drug, and consequently with dosages of the formulated product. He does not seek to control the amount of lipid liposome component that is administered to a patient except insofar as that is a factor in delivering the encapsulated drug. In contrast, in Rubin, the phospholipid is being used as an active substance per se. Thus, one skilled in the art reading Rubin would not have been prompted to modify the liposomes in view of the entirely different direction of Rubin.

30. Moreover, as noted above, modification of the liposomes of Radhakrishnan to increase the ratio of lipid to drug would have been considered to be subject to the significant constraints of maintaining satisfactory liposome formation and, more importantly, maintaining efficacy and reproducibility of dosage of the active drug. Modifying the liposomes of Radhakrishnan to have a lipid component according to Rubin would at best have a very unpredictable effect on the liposome performance. The liposomes would be affected in two main respects:

- The controlled release characteristics would be affected by adopting the lipid composition of Rubin, and it is by no means clear that liposomes would be formed (and

absence of liposome formation would further deter the reader of Radhakrishnan from proceeding with modification according to Rubin.)

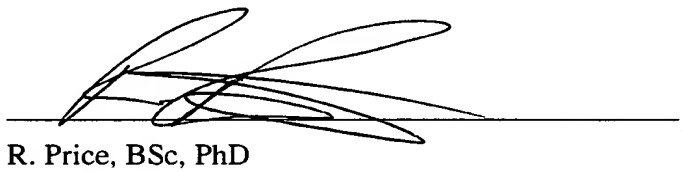
- The inevitable reduction in drug loading per liposome would lead to greater numbers of liposomes having a limited amount of drug and to problems with dose reproducibility in relation to the drug.

It is further noted that Rubin discloses only suspensions of lipid. It is a particular advantage of the present invention that the phospholipid is a dry finely-divided powder that enables much larger amounts of phospholipid to be aerosolised in individual doses (for example, by a dry powder inhaler, or by embracing the dry powder in a stream of propellant within a dispensing device). That enables the phospholipid component used in accordance with the invention to be incorporated in a hand-held, portable device and offers further advantages in terms of comfort and convenience to the patient as compared with a nebuliser as described in Rubin.

31. In summary, considering Radhakrishnan, Mautone and Rubin, both separately and in combination, a person in this field would not have been motivated to provide an antiasthma drug in combination with a phospholipid composition in dry, finely-divided form, and with large doses of phospholipid composition. Moreover, these three documents would not provide such a worker with a reasonable expectation of success in permitting treatment to be carried out with reduced side effects. In contrast, the reasoning and data in the captioned patent application now make available to those working in this field valuable methods of treatment of asthma, with convenient and simple products with the potential for enhanced convenience for the patient and thus for improved patient compliance.

32. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardise the validity of the referenced application or any patent issued thereon.

15/03/04
Date



R. Price, BSc, PhD

Dr ROBERT PRICE

B.Sc. (Hons), PhD (Wales)

PERSONAL

Date of Birth:	26th August 1970
Nationality:	British
Marital Status:	Married

EDUCATION AND QUALIFICATION

1991 – 1994	University of Wales College of Cardiff
	PhD in Physical Chemistry (Prof. G.A. Attard)
1988 – 1991	University of Wales College of Cardiff
	B.Sc.(Hons) Physics: Class 2(i).
1981 – 1988	Ysgol Gyfun Ystalyfera, Wales

CURRENT POSITION

2000 -	Pharmaceutics Lecturer, Department of Pharmacy & Pharmacology, University of Bath, Bath, BA2 7AY. United Kingdom.

PREVIOUS POSITIONS

1998 - 2000	University of Bath, Department of Pharmacy
	Postdoctoral research associate (Prof. J.N. Staniforth)
1997 – 1998	University of Bath, Department of Materials Science
	Postdoctoral research associate (Dr. P.J. Halfpenny)
1996 – 1997	University of Southampton, School of Chemistry
	Postdoctoral research associate (Prof. B.E. Hayden)
1995 - 1996	University of Bath, Department of Materials Science
	Postdoctoral research associate (Dr. P.J. Halfpenny)
1994 - 1995	University of Wales College of Cardiff

POSTGRADUATE SUPERVISION (HIGHER RESEARCH DEGREES)

Degree	Current No. of Students	No. of Students Completed
PhD	7	1
PDRA	2	-

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RESEARCH ACTIVITIES

Summary of current research

My research interests have focussed on investigating the physico-chemical properties which govern particle adhesion, surface stability issues of processed particles and the general areas of particle technology and crystal growth. Specific interests include: (a). particlate interactions in dry powder inhlation formulations and suspension based pressurised metered dose inhaler formulations; (b). development, processing and optimisation of formulations for inhalation systems; (c) development of novel particle engineering and processing techniques, and; (d). surface energetic and surface stability properties of active pharmaceutical ingredients.

PUBLICATIONS

Academic Journal Publications (2002-2003)

Visualisation of the Crystallisation of Lactose from the Amorphous State
R Price and P M Young
Journal of Pharmaceutical Sciences (2003 *in press*)

The Influence of Relative Humidity on the Cohesion Properties of Micronised Drugs used in Inhalation Therapy
P M Young., R Price., M J Tobyn., M Buttrum., F Dey.
Journal of Pharmaceutical Sciences *(*2003 *in press)*

Effect of Relative Humidity on the Aerosolisation of Micronised Drugs
P M Young, R Price, M. J. Tobyn., M. Buttrum., F. Dey.
Drug Development and Industrial Pharmacy *(*2003 *in press)*

The Effect of Mechanical Processing on Surface Stability of Pharmaceutical Powders: Visualisation by Atomic Force Microscopy
P Begat, P. M. Young, S. Edge, J. S. Kaerger and R. Price
Journal of Pharmaceutical Sciences (2003) **92:** 611-620

Under Pressure: Predicting Pressurised Metered Dose Inhaler Interactions Using the Atomic Force Microscope
P M Young, R Price, D Lewis, S Edge, D Traini
Journal of Colloid and Interface Science (2003) **262:** 298-302

Investigation into the Effect of Humidity on Drug-Drug Interactions Using the Atomic Force Microscope
P. M Young., R. Price., M. J. Tobyn., M. Buttrum., F. Dey.
Journal of Pharmaceutical Sciences (2003) **92:** 815-822

Characterisation of a Surface Modified Dry Powder Inhalation Carrier Prepared by "Particle Smoothing"
P. M. Young., D. Cocconi., P. Colombo., R. Bettini., R. Price., D. F. Steele., M. J. Tobyn.
Journal of Pharmacy and Pharmacology (2002) **54:** 1339-1344.

The Influence of Relative Humidity on Particulate Interactions In Carrier Based Dry Powder Inhaler Formulations
R. Price., P.M. Young., S. Edge., J. N. Staniforth.
International Journal of Pharmaceutics (2002) **246:** 47-59

Chemical Characterisation of Sodium Starch Glycolate Particles.
S. Edge., A. M. Belu., U. J. Potter., D. F. Steele., P. M. Young., R. Price., J. N. Staniforth.
International Journal of Pharmaceutics. (2002) **240:** 67-78

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Academic Journal Publications (1994 - 2001)

R. Price, G.R. Ester, P.J. Halfpenny, **Proceedings of the Royal Society of London A, 455** (1999) 4117.

G.R. Ester, R. Price, P.J. Halfpenny, **J.Phys. D: Appl. Phys. 32** (1999) 128.

R. Price, G.A. Attard, **J. Electroanal. Chem. 467** (1999) 60

G.R. Ester, R. Price, P.J. Halfpenny, **J. Crystal Growth 187** (1997) 95.

R. Price, G.A. Attard, A. Al-Akl, **Surface Science, 335** (1995) 52.

R. Price, G.A. Attard, **Surface Science, 336** (1995) 63.

R. Price, G.A. Attard, **Electrochimica Acta., 39** (1994)1525.

INVITED ORAL PRESENTATIONS

Pharmaceutical Surface Science: Applications to drug-polymer interactions in inhaled systems
R. Price
Presented at XVII Helsinki University Congress on Drug Research, July 2003, Finland.

Physico-chemical interactions in inhaled products.
R. Price
Presented at Advanced Pharmaceutical Sciences meeting, February 2003, London, UK.

Characterisation of the surface physico-chemical stability of materials directly applicable to inhalation therapy.
R. Price
Presented at Drug Delivery to the Lungs XIII, December 2003, London, UK.
Abstract: Journal of Aerosol Medicine Vol 16 (1) 2003

Variations in Particle Adhesion in carrier based dry powder inhaler (DPI) formulations
R. Price
Presented at World Congress in Particle Technology, July 2003, Sydney, Australia.

DPI Powder Adhesion Properties: The Power of AFM.
R. Price
Presented at Respiratory Drug Delivery VIII, May 2002, Tucson, Arizona, USA.

Probing Inter-particulate Forces.
R. Price
Presented at Particles 2002, April 2002, Florida, USA.

Magazine Articles

Environmentally Controlled Optical Microscopy for the Pharmaceutical Sciences
P. M. Young, J. Booth and R. Price
Microscopy and Analysis (2003) May issue

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Conference Proceedings

Using Raman spectroscopy for polymorph differentiation and chemical imaging.
R. Price, T. Smith, D. F.Steele, S.Terras, P. M.Young.
The 3rd European Academy of Forensic Science (EAFS) Triennial Meeting and Exhibition Sept 2003, Istanbul, Turkey

Visualisation of Pharmaceutical Material Surface Stability as a Function of Mechanical Processing
P, Begat, R. Price, P. M. Young.
Data presented at APS Inhalation, February 2003, London, UK

The use of a novel 'active' inhalation device to deliver high respirable fractions of high dose dry powder active agents to the lung.
P. M. Young, J. Thompson, R. Price, D. Woodcock K. Davies.
Data presented at ISAM, International Congress on Aerosols in Medicine. June 2003, Baltimore, USA.

Pre-Formulation Characterisation of Dry Powders For Inhalation by Atomic Force Microscopy: The Effect Of Relative Humidity On Particle Cohesion.
Paul M Young, R. Price, M. J. Tobyn, M. Buttrum, Fiona Dey.
Data Presented at Respiratory Drug Delivery VIII, May 2002, Tucson, Arizona, USA.

Inhalation Mixtures of Anti-asthmatic Drugs with Smoothed Lactose.
D. Cocconi, C. Penotti, R. Bettini, P. Young, R. Price, P. Colombo, C. Marriott.
Data Presented at Respiratory Drug Delivery VIII, May 2002, Tucson, Arizona, USA.

The Study of Force Control Additives in Creating High-Performance Dry Powder Inhaler Formulations.
D. V. Morton, M. Green, J. N. Staniforth, P. Begat, R. Price, P. M. Young.
Data Presented at Respiratory Drug Delivery VIII, May 2002, Tucson, Arizona, USA.

Use of AFM to elucidate humidity induced changes in interparticle adhesion in dry powder inhaler systems.
R. Price, P. Young and M.J. Tobyn
Data Presented at Particles 2002, April 2002, Orlando, Florida

Surface Topography and Adhesive Forces of a Surface-modified dry powder inhaler formulation Technology
D. V. Morton, M. Green, J. N. Staniforth, P. Begat, R. Price, P. M. Young.
Data Presented at Particles 2002, April 2002, Orlando, Florida

Predicting Pressurised Metered Dose Inhaler Performance and Stability using the Atomic Force Microscope.
D. Traini, P. M. Young, R. Price
Data presented at AAPS Annual Meeting and Exposition October 2002 Toronto, Canada.

Use of Raman Mapping to Investigate in-vivo Deposition of a Combination pMDI Asthma Therapy
D. F. Steele, P. M. Young, T. Smith, D. Lewis, R. Price.
Data presented at AAPS Annual Meeting and Exposition October 2002 Toronto, Canada.

Novel Production of Crystalline Particles with a Respirable Size Range
J. S. Kaerger, R. Price, P. M. Young
Data presented at AAPS Annual Meeting and Exposition October 2002 Toronto, Canada.

Characterisation of the surface physico-chemical stability of materials directly applicable to inhalation therapy: The power of AFM
R. Price, P, Begat, P. M. Young.
Data presented at Drug Delivery to the Lungs XIII, December, 2002 London, UK.
Abstract: Journal of Aerosol Medicine Vol 16 (1) 2003

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The Potential Roles of The Atomic Force Microscope Colloid Probe Technique in Pre-formulation Screening
P. M. Young, R. Price, M. Tobyn.
Data presented at Drug Delivery to the Lungs XIII, December, 2002 London, UK.
Abstract: Journal of Aerosol Medicine Vol 16 (1) 2003

Characterisation of the Electrostatic Properties of pMDI Formulations via Electrostatic Low Pressure Impactor (ELPI) Measurements.
R. Hopkins, P.M. Young, D.A. Lewis M.J. Tobyn, and R. Price.
Data presented at ISAM, 13th International Congress on Aerosols in Medicine. September 2001, Interlaken Switzerland.

Direct Visualisation of the Re-crystallisation Processes of Amorphous Spray Dried Particles.
R. Price, P. M. Young
Data presented at AAPS Annual Meeting and Exposition October 2001 Denver, CO, USA.

An Atomic Force Microscope Investigation of the Effect of Relative Humidity on Adhesion Properties of Pharmaceutical Powders.
Paul M Young, M. J. Tobyn, R. Price, M. E. Butrum, F. Dey
Data presented at AAPS Annual Meeting and Exposition October 2001 Denver, CO, USA.

Surface Topography and Electrostatic Interactions of a Novel High Performance Dry Powder Inhaler Formulation Technology: PowderHale™.
D. A. Morton, P. Begat, M. Green, J. N. Staniforth, R. Price, P. M. Young
Data presented at AAPS Annual Meeting and Exposition October 2001 Denver, CO, USA.

The Use of Atomic Force Microscopy in Determining Physical Properties of Pharmaceutical Powders
Paul M Young, M. J. Tobyn and M. E. Butrum
Data presented at AAPS Annual Meeting and Exposition, October 2000 Indianapolis, IN, USA

Towards the direct measurement of the interaction forces acting between micronised particles and pharmaceutically relevant substrates using atomic force microscopy.
R. Price, J.N. Staniforth, M. Thomas and M.B. Davies
Data presented at AAPS Annual Meeting and Exposition October 2000 Indianapolis, IN, USA.

Variation in Particle Adhesion due to Capillary and Electrostatic Forces.
R. Price, J.N. Staniforth, M. Thomas and M.B. Davies.
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